Epidemic Outbreak Surveillance (EOS)

An Advanced Concept Technology Demonstration ACTD

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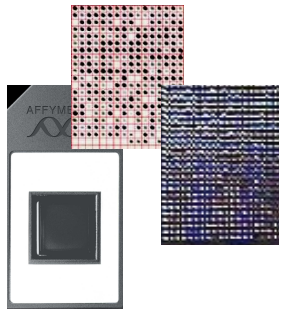
Synonyms for the EOS Z-chip Technology

- DNA Array
- DNA Microarray
- DNA Chips
- Gene Chip
- Genome Chip
- Protein Microarray
- Protein Chip



New 'DNA Chip' Rapidly Detects, Identifies Dangerous Pathogens

Affymetrix (AFFX)	AxyS (AXPH)	Caliper (CALP)
Celera (CRA)	Corvas (CVAS)	CuraGen (CRGN)
Gene Logic (GLGC)	Geneset (GENXY)	Genzyme Mol. Oncol. (GZMO)
GSI Lumonics (GSLI)	Hyseq (HYSQ)	Incyte (INCY)
JMAR (JMAR)	Lynx (LYNX)	Nanogen (NGEN)
Sequenom (SQNM)	SurModics (SRDX)	Vysis (VYSI)
Xenometrix (XENO)	Genomic Solutions (GNSL)	Orhcid BioSciences (ORCH)

What is a Microarray?

- Semantically “MICROARRAY”
  - Micro:
    - <200 μm spots of 10^7-10^8 DNA, cDNA, or oligo copies
    - Capacity for up to 30,000 genes or 500,000 Dx tests per chip High throughput analysis of DNA, protein, or gene
  - Array:
    - An orderly arrangement of samples

- The “microarray chip” is a small glass, nylon or silicon chip that match thousands of known and unknown DNA samples simultaneously

- *Cutting Edge* of functional genomics

Chip Manufacture

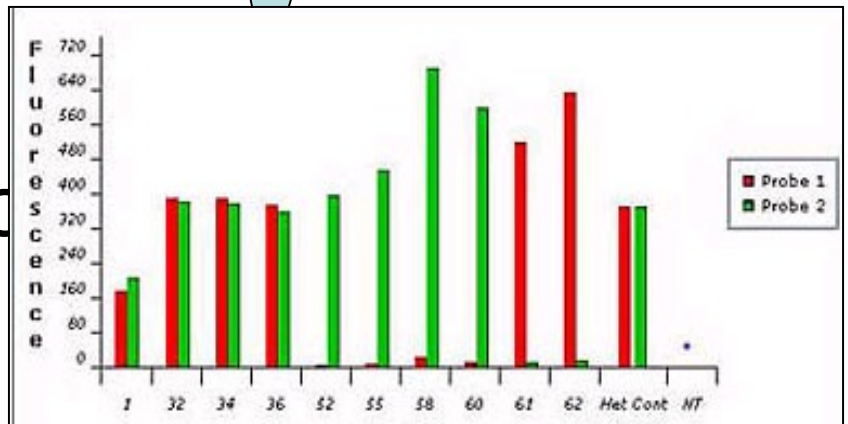
- Microscope slide sized plate (glass, silicon or nylon)
- Human Genome.
- Robotic manufactur
- Location of each gene identified in the spot.
- As many as 300K comparisons available for evaluation.

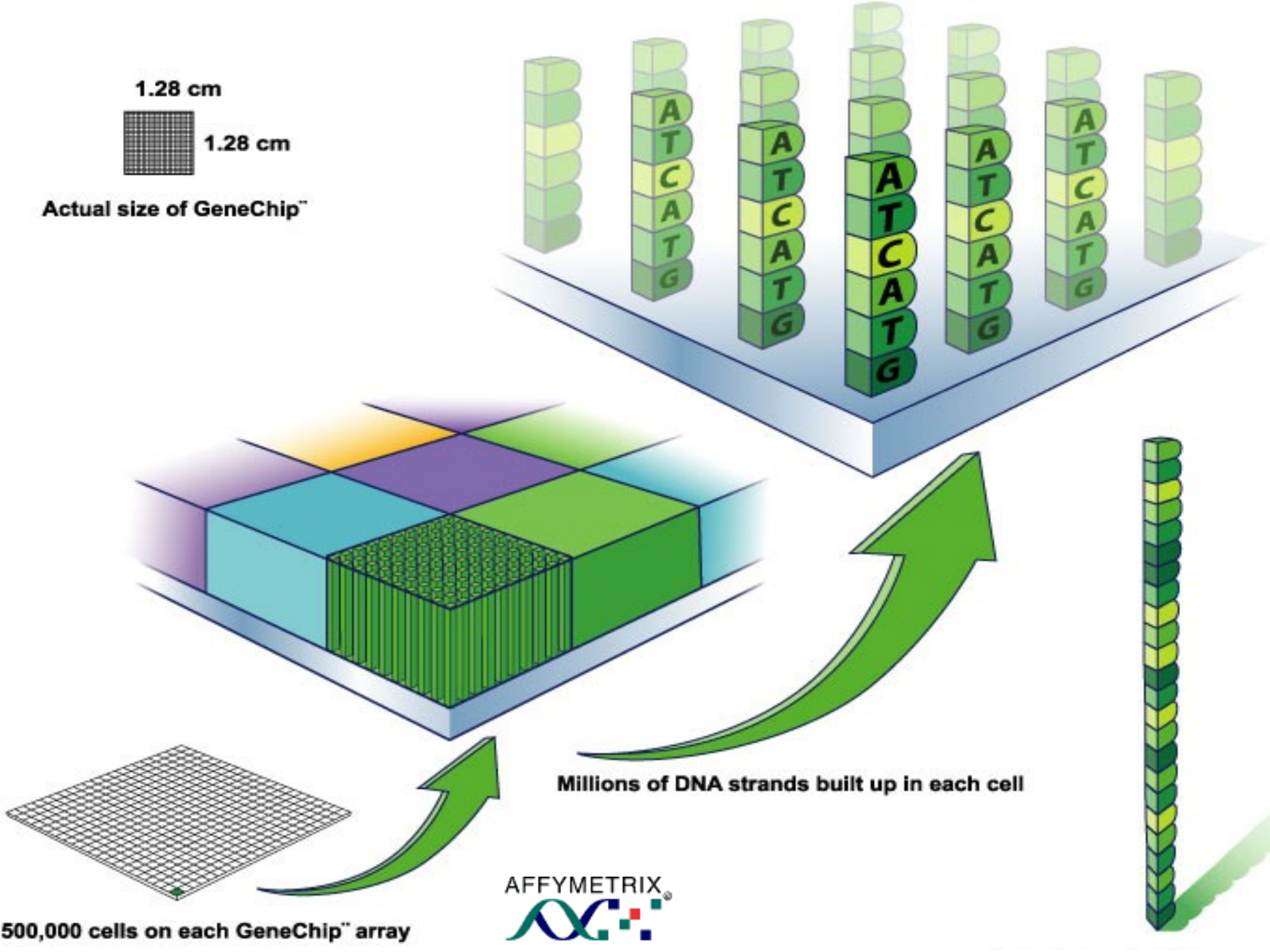
Genetics 101

- Everybody has basically the same genes.
- 4 bases are involved in DNA (A-T and C-G)
- The key is whether the genes are turned on “expressed”.
- Most cell types carry the complete DNA sequence.
- Disease states impact different genes with regard to on/off or amount of expression.

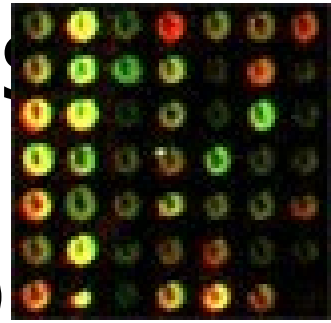
Microarray Process

- Prepare *target* sample
  - cDNA
  - Fluors
- Hybridize
  - Wet chemistry
  - 4 possibilities
- Scan
- Analyze/Informatic

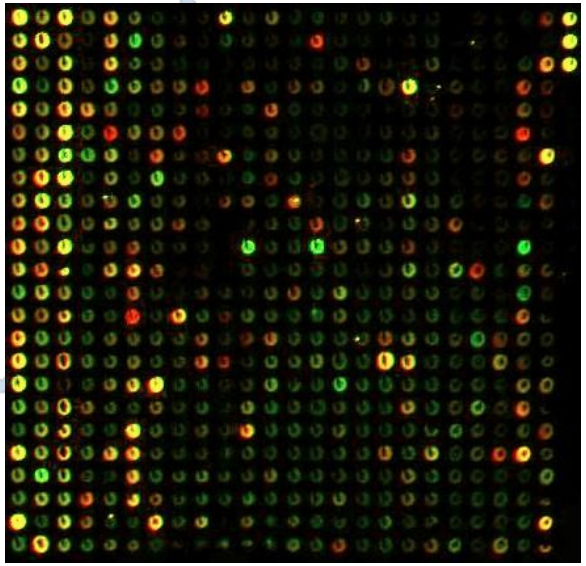



1.28 cm
1.28 cm
Actual size of GeneChip™
A T C A T G
Millions of DNA strands built up in each cell
500,000 cells on each GeneChip™ array
AFFYMETRIX®

Microarray Applications

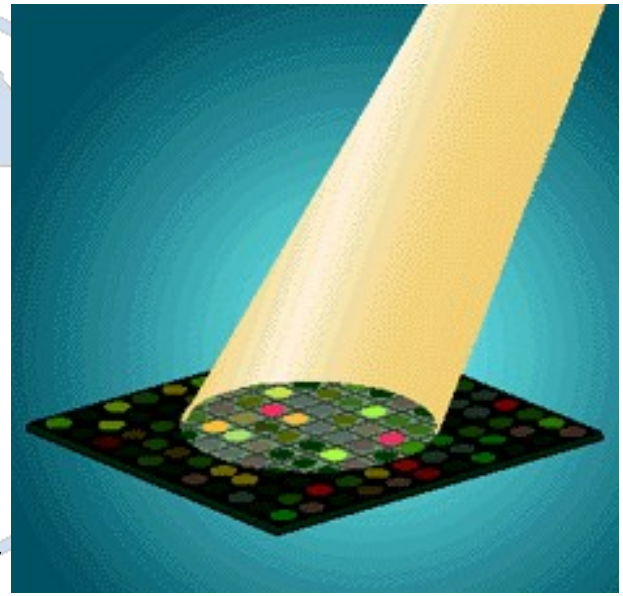


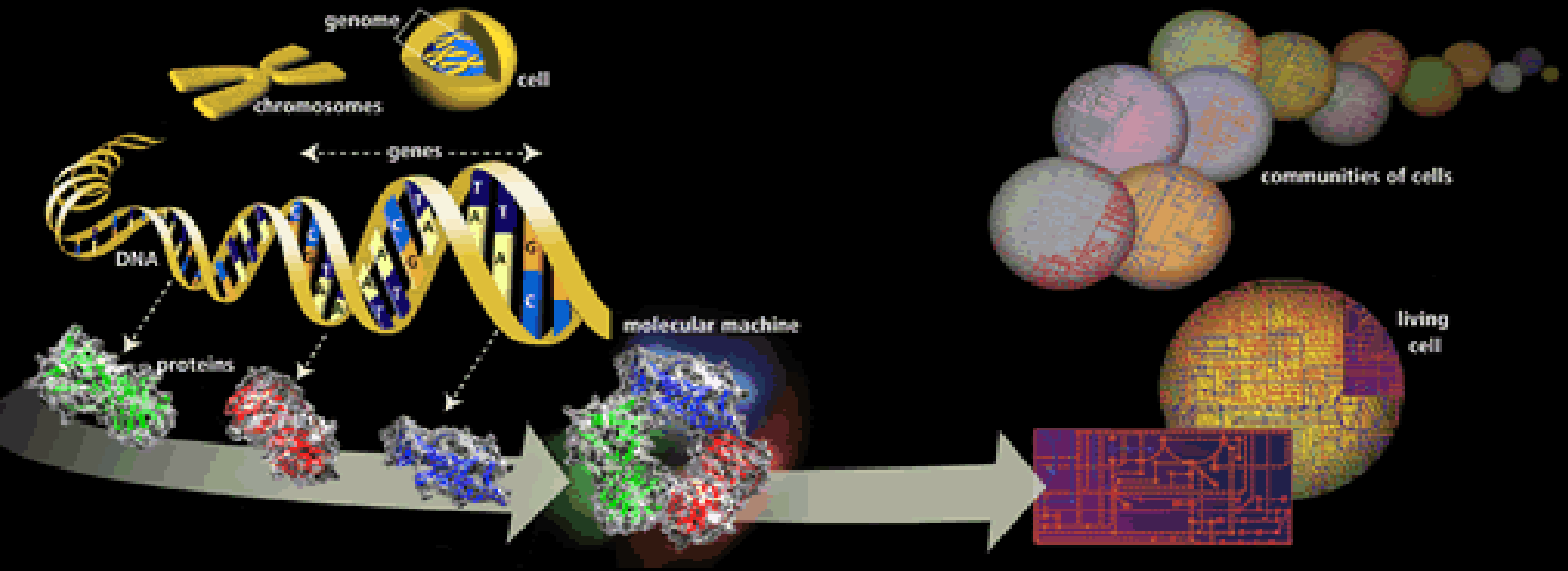
- Gene discovery
- Gene expression profiling (agent & host)
  - Detect individual susceptibility
  - Detect acute phase response
- Diagnostics
  - Microbial identification
  - Microbial genotyping
  - Antibody detection
    - Protein arrays via microfluidics
  - Tumor profiling
    - Tissue microarrays
- Drug Discovery: “pharmacogenomics”
- Toxicologic Research: “toxicogenomics”



Microarray Technology

- Compilation of
  - KNOWLEDGE
    - Human Genome Project
  - TECHNOLOGY
    - DNA hybridization
    - LASER
    - Microfabrication Technology
  - APPLICATION
    - Solutions for real-world challenges
    - Co-development with Syndromic Surveillance
- An *ENABLER*, not a *PANACEAE*





...from DNA to life

Human Genome Project Information

Genomes to Life

Microbial Genome Program

US Developing Biological Early Warning System

- 20 November – Reuters Health reported the US military, backed by civilian health authorities, is developing and beginning to deploy an **early warning system** for possible biological attacks, a conference on defending against biological warfare heard on Tuesday. The technique, known as "syndromic surveillance," incorporates data from hospitals, clinics, pharmacies, schools and even veterinarians into a single source to detect whether there has been a surge in any infectious disease.

Joint Requirements Matrix

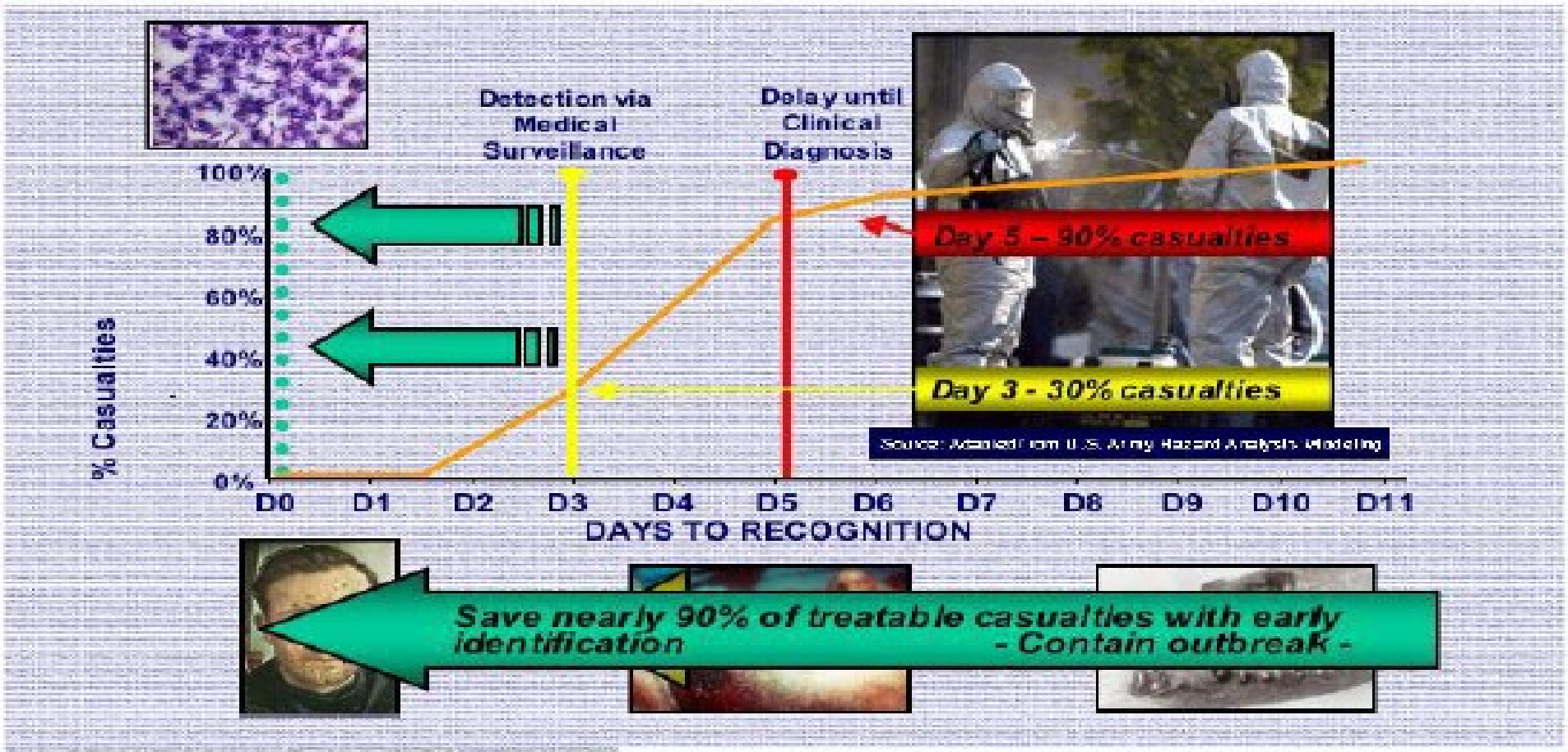
- Non-platform dependent, capabilities-based requirement

CJCS Vision – Force Health Prot ***Joint Biological Agent ID and Diagnostic System (JBAIDS) ORD***	***•Provide Preventative Measures, Diagnosis, Treatment of Disease and Injury.*** •Casualty prevention-from environment and enemy action) •Casualty care and management-mobile, lighter, faster, responsive medical capability ***•Maintain an integrated medical surveillance system (first responder to definitive treatment)*** ***•Provide timely, accurate ID of biological agents to support clinical and operational decision-making, and data archiving*** ***•Advanced diagnostic platforms-multiplex, near real time*** ***•Integration of diagnostics and informatics***

Epidemic Outbreak Surveillance (EOS) ACTD

EOS ACTD Program

- Develop Comprehensive Medical Surveillance Capability.
- Develop an advanced diagnostic capability for biowarfare and common pathogens.
- Save 90% of treatable casualties; contain outbreak within 2-3 days.
- Develop a data fusion capability to assist operational and clinical decision making supporting biodefense and military medicine.
- Provide a comprehensive Joint Employment Concept of Operations to enhance operational readiness and mission execution.



Epidemic Outbreak Surveillance (EOS) ACTD

A System of Systems Approach

Clinical Medicine

Operational AF Benefits

- High-Density DNA Microarrays
- Genomes and Gene Expression
- Integrated Network IT
- Gold-Standard Epidemiology
- Proactive ELSI Support
- Real World Outbreak Model

Epidemic Outbreak Surveillance (EOS) ACTD

Advanced Diagnostics

Operations and Deliverables

Respiratory Pathogen Microarray (RPM)

Z-chip from concept to delivery
(Operational from 07 Jun 2003)
Common and biowarfare agents
Iterative design and process
Delivery, evaluation, and validation

Common Pathogens

- Adenovirus
- Influenza
- Coronavirus
- West Nile
- Parainfluenza
- RSV
- Rhinovirus
- Strept. pyogenes
- Chlam. pneumoniae
- Myco . pneumoniae
- Bord. pertussis
- Neiss. meningitidis
- Strept. pneumoniae

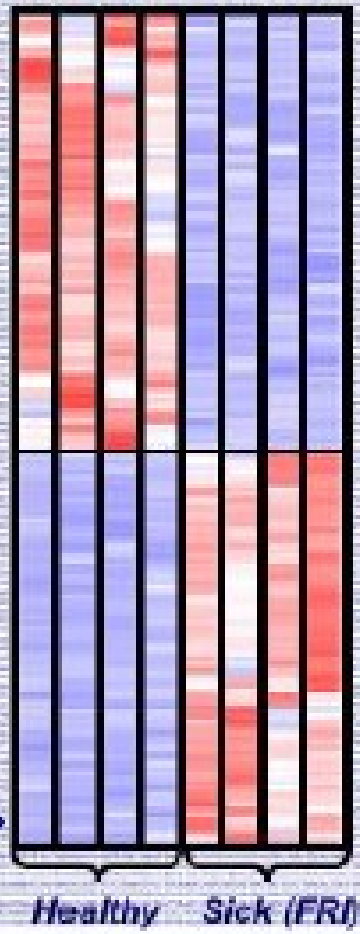
Biowarfare Pathogens

- Smallpox
- Anthrax
- Plague
- Tularemia
- Ebola Virus
- Lassa Fever

Host Response Gene Expression Profiles

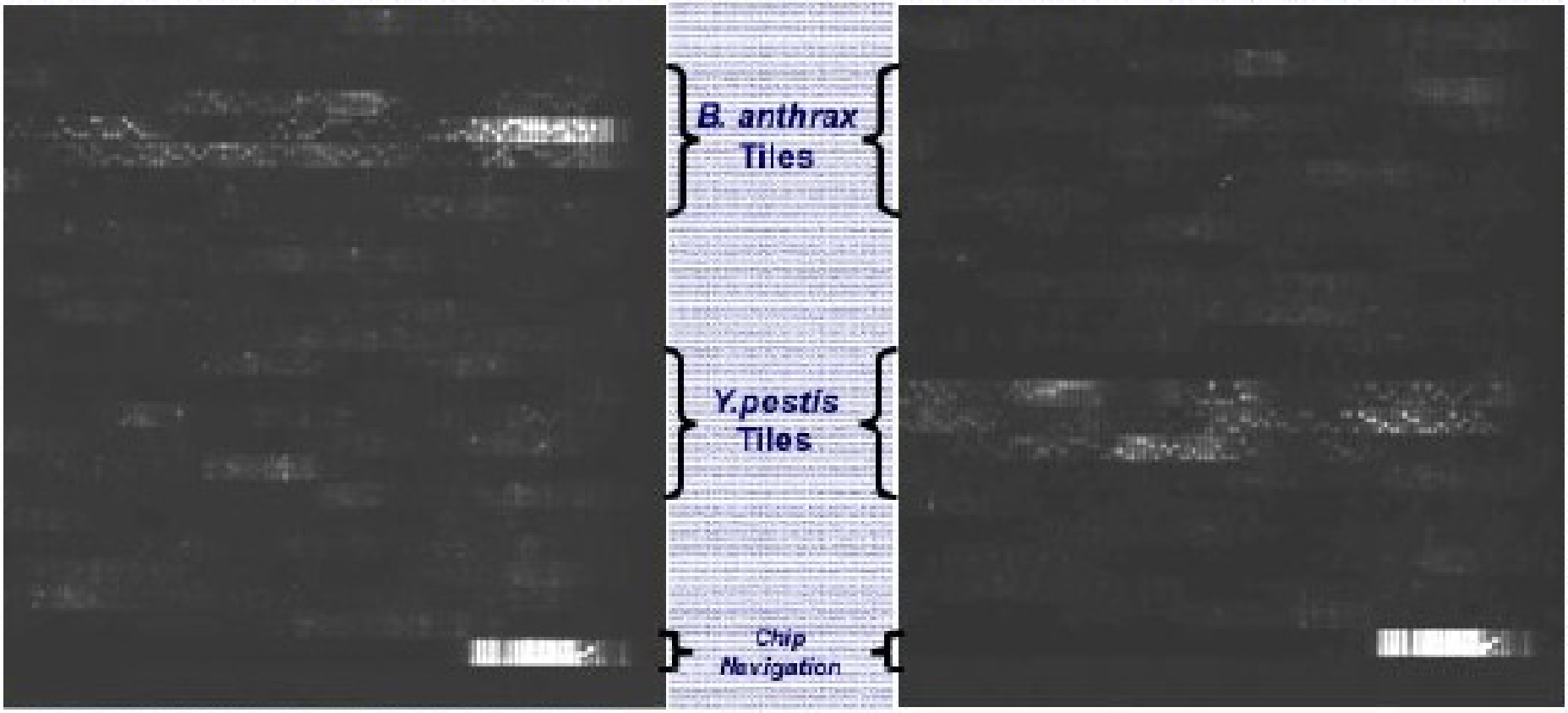
Up to 500,000 diagnostic tests per chip

Over 30,000 human genes per test



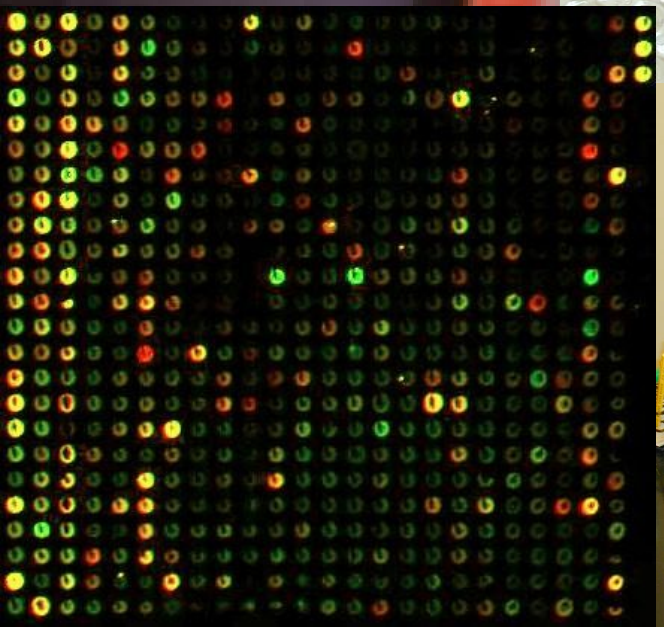
Zebra-Chip
B. anthracis vs. Y. pestis

- Single test distinguishes biowarfare agents of "flu-like" syndrome
- Total DNA amplification (no specific primers!)
- Assay on EOS Respiratory Pathogen Microarray (RPM)
- Approaching objective: Decision-quality information in 2 hours



Microarrays: where are we now?

- “Technology with longer time-line to fruition” Donald Jungkind, Thomas Jefferson University
- “This technology is still considered to be in its infancy” National Center for Biotechnology Information
- Migration from research bench to clinical lab
  - Long path to mass production and FDA approval
  - Creative phase Production scale-up
  - Improve accuracy, workflow, expense, durability
  - Develop an array of applications
- Cross-Cutting interest and funding



Acknowledgments

- COL Marc Mattix, DVM
- Leming Shi, PhD

QUESTIONS

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